

IN THE SPECIFICATION:

Please replace the following paragraph at page 5, lines 25-32:

Drug metabolizing enzyme antibody microarrays were produced using purified immunoglobulins (IgG) as well as fluids unprocessed for IgG isolation, e.g., anti-sera or ascites fluids. They were used to analyze ~~Analyzing~~ protein expression of hepatic proteins obtained after phenobarbital treatment of rats ~~was determined~~. Twelve up-regulated proteins after phenobarbital treatment were identified by the antibody microarray. It was surprising that, in Western blot analysis, only 1 out of the 12 up-regulated proteins failed to show increased protein expression.

Please replace the following paragraph at page 7, lines 15-38:

Generally, the present invention relates to a microarray including a substrate on which a plurality of sample spots is arranged in a two-dimensional array. The present invention provides a method of producing antibody drug-metabolizing enzyme antibody microarrays. Specifically, the present invention relates to microarrays including closely related cytochromes P450. The present invention also relates to producing antibody chips with fluids that are not processed for immunoglobulin isolation including anti-sera, ascites fluids, and hybridoma culture media. The present invention relates to analysis of levels of spotted IgG by hybridization of labeled secondary IgG to decide optimal antibody levels to spot on the slide. Use of a spiked internal control to normalize microarray data obtained from focused (non-global) array analysis is also disclosed. Further, the present invention provides a method to increase signal with array analysis using an intensive molecular signal.

Please replace the following paragraph at page 7 line 29 to page 8 line 3:

The microarray of the present invention can be produced using monoclonal and polyclonal antibodies ~~with IgG~~ as purified immunoglobulins as well as fluids that

are not processed for immunoglobulin isolation, including anti-sera, ascites fluids and hybridoma culture media. According to the present invention a method is disclosed to increase signal strength of array analysis utilizing intensive molecular signals. Further, the present invention relates to production of drug-metabolizing enzyme antibody microarrays. The present invention also provides a method of producing drug-metabolizing enzyme antibody microarrays including closely related cytochromes P450.

Please replace the following paragraph at page 13, lines 6-15

Anti-Flag IgG, which recognizes Flag protein, an internal control protein for Cy3 and Cy5 conjugation and hybridization, was ~~were~~ spotted three times in each block (top and bottom blocks). Prior to Cy3 and Cy5 conjugation, 2 µg of the Flag landmark protein was spiked to 1 mg of protein. After hybridization of the chips with the probe, signal strength of each spot was obtained. Ratios of signal strength of Flag protein spiked in control and protein obtained from phenobarbital treated rats were 9.7 (mean of 1.2, 0.9, and 0.8) and 1.0 (mean of 1.1, 1.1 and 0.9) for 50 and 500 µg/ml IgG spots, respectively (Table. 3). The mean ratio was used as a normalization factor (NF) for the array analysis.

Please replace the following paragraph at page 14 line 23 to page 15, line 3:

In order to further demonstrate the effectiveness of the present invention, Ggene Sspring™ analysis of 500 µg/ml antibody spots is shown in Figure 2. The middle diagonal line is for a protein expression level that did not change after PB treatment, the top line is for 2-fold increase, and the bottom line is for 2-fold decrease. Internal control, Flag proteins (3 sets) (2 µg), spiked to 1 mg of sample, were close to the middle line as expected and showed high signal values (mean value, 2663). GST-alpha and antioxidant-like protein 1 also

showed high expression levels without any change. CYP2B1 and CYP2B1/2B2 spots were above the 2-fold increase line with 9.3- and 9.7-fold increase, respectively, after PB treatment. CYP2B1 was reported to be a primary protein that increased after PB treatment. An interesting observation is that both CYP2B1 IgG and CYP2B1/2B2 IgG bound with CYP2B1 protein.